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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,967	02/15/2002	William E. Rich	016866-005710US	1477

20350 7590 03/23/2004

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EXAMINER
CLOW, LORI A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,967	RICH ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *21 Oct 2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-30 are currently pending in the instant application.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. For example see page 49, lines 18-21.

Information Disclosure Statement

The Information Disclosure Statement filed 21 October 2002 has been considered. A signed copy of PTO Form 1449 is included with this Office Action.

Claims Objections

Claim 5 is objected to for containing a typographical error. The second line should read "cell lysate from a cell of a subject who responds to a drug treatment".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

Claims 1-16, 18-28, and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying specific physio-chemical properties such as amino acid sequence or isoelectric point for fractionation, does not reasonably provide enablement for **any** physio-chemical property used for fractionation of polypeptides. In

the event that a physio-chemical property equated to an **activity**, how does one fractionate based upon that activity? The specification provides enablement for properties such as amino acid sequence, molecular weight, isoelectric point, hydrophobicity, hydrophilicity, glycosylation, phosphorylation, epitope sequence, ligand binding sequence, charge at a specified pH, and metal chelate binding. However one of skill in the art would not be able to practice the said invention using any known biological or chemical activity. For example, how would one separate or fractionate a polypeptide based upon an atomic spin property, which is a physio-chemical property?

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or

absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to correlate gene expression and protein expression in a biological sample by obtaining a sample; generating a gene expression profile, thereby identifying an mRNA expressed in the sample; identifying a physio-chemical property of a polypeptide encoded by the mRNA; fractionating the polypeptide based on the physio-chemical property; and identifying the polypeptide encoded by the mRNA from among the fractionated proteins, thereby correlating gene and protein expression.

For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification provides general examples of various gene expression profiling techniques which are well known in the art. For example at page 18, the specification states that the methods for examining gene expression include northern blots, dot blots, and PCR related techniques, and nucleic acid arrays. The specification then describes the various physio-chemical properties of amino acids and how they may be used to fractionate proteins for analysis, also techniques well known in the art. Finally the specification states that once the polypeptides are fractionated a next step is to identify a polypeptide from among the fractionated polypeptides that corresponds to the polypeptide encoded by the selected mRNA and somehow correlate this to gene expression.

However, there is nothing in the claims or in the specification that would guide one of skill in the art to practice this invention because it is not defined how one goes from the step of

generating a gene expression profile of mRNA that is expressed to identifying a physio-chemical property of a polypeptide encoded by the mRNA and thereby correlating gene and protein expression in this step-by step way. How does one go from step (b) to step (c) without actually having the protein? How does one identify a physio-chemical property of the polypeptide encoded by the mRNA when all one has is the mRNA? No link has been established for doing so.

Secondly, how does one correlate gene expression with protein expression considering there is a diversity of proteins which can be generated from a single gene due to differential splicing, for example (post-transcriptional changes)? There is not a strict linear relationship between genes and proteins.

The specification sites no working examples of the invention.

d) The invention is drawn to methods for correlating gene expression with protein expression.

e) and g) The prior art indicates that the activity state of a protein often depends on its modification state. i.e. post-translational modification, multiple initiation sites, abnormal termination etc. Furthermore, the expression of a gene may be the same in two situations. However the protein expression may not. For example, if the protein is phosphorylated or de-phosphorylated, this may indicate an active protein under one set of conditions or an inactive protein in the other. The prior art indicates that the number of genes in the human genome that are expressed easily reach 20,000. However, the actual numbers of proteins that are expressed reach far greater numbers. One of skill in the art would not know how to correlate gene

expression levels with protein expression levels using the steps presented in the in the instant specification. (see Huber in Nature (2003) Vol. 4, pages 74-80 for a review of proteomics).

f) The skill of those in the art of molecular biology and protein chemistry is high.

The skilled practitioner would first turn to the instant specification for guidance to practice methods of correlating gene and protein expression. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that would require substantial additional work and research. Finally, said practitioner would turn to trial and error experimentation to determine whether the mRNA could reliably be used to identify a physio-chemical property of a protein, without the actual protein and that protein and gene expression could be correlated using this method. Such represents undue experimentation.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (571) 272-0549.

MARJORIE MORAN
PATENT EXAMINER
3/20/04

March 19, 2004

Lori A. Clow, Ph.D.
Art Unit 1631